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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,693	11/09/2006	Takashi Yamashita	Q95455	4348

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
05/13/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,693	YAMASHITA ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/2/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 25-30* is/are pending in the application.

4a) Of the above claim(s) *7-23 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 2, 2009 that includes a response to the office action dated October 3, 2008, has been entered. No claims were amended, cancelled or newly added. Claims 1-23 and 25-30 are currently pending in the application. Claims 7-23 and 28-30 remain withdrawn from consideration, without traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. Claims 1-6 and 25-27 are under current examination. The claims have been examined commensurate in scope with the elected species of chicken.

Response & Maintained Claim Rejections - 35 USC § 102

Claims 25-27 stand rejected under 35 U.S.C. 102(e) as being anticipated by Ransohoff et al. (U.S. Patent Application Publication 2003/0176660; effective filing date Feb. 8, 2002). The rejection set forth on page 5 of the office action dated March 19, 2008, and pp. 3-4 of the previous office action dated October 3, 2008 is maintained for reasons of record.

The previous office action indicated that the process steps recited in claim 1 result in transgenic chimeric chickens, especially when mating G0 chimerics to another unrelated G0 chimeric chicken, or a wild-type bird. Thus, germline transmission of the transgene is not necessarily achieved, and hence the transgene need not be present in the egg. Moreover, the instant claims are directed to an egg laid by a chicken, containing varying amounts of a desired protein, therefore the features upon which applicant relies (i.e., Moloney murine leukemia-specific sequences) are not recited in the rejected claim(s). Thus, the claimed chicken of base

claim 1 has been interpreted to be a chimeric chicken in view of the method steps recited in the claim.

Applicants disagree and traverse, arguing, that claim 1 recites a "transgenic bird ... which is obtained as a G1 transgenic bird or an offspring thereof." Thus, contrary to the Examiner's position, Claim 1 is not directed to the offspring from GO transgenic chimeras that do not contain the transgene, which are, by definition, not transgenic birds. Rather, the transgenic bird of Claim 1, by virtue of being a G1 transgenic bird (or transgenic offspring thereof'), logically would produce eggs containing the transgene and the MMLV-derived vector sequences, because the production of G1 transgenic birds involves germline transduction of the transgene. Applicants' arguments have been fully considered, but are not deemed persuasive.

In response, it should be noted that the distinction between a chimeric and a transgenic chicken cannot be blurred, despite Applicants' use of the term transgenic chimeric. Base claim 1 is a product by process claim, wherein the process comprises the method steps of mating a G0 transgenic chimeric bird with any other G0 transgenic chimeric bird or a with a wild type bird. By definition, a G0 chimeric bird carries the transgene in only some of its somatic cells and is not capable of germline transmission of the transgene. Thus crossing a chimeric bird with a wild type bird or a non-related chimeric bird, would further dilute the transgene and cannot result in the production of a true transgenic bird. Therefore, in view of the process steps recited in base claim 1, the resulting product has been correctly interpreted as a chimeric bird.

Applicants cite MPEP 2143.03, that all words in the claim must be considered in judging the patentability of that claim against the prior art. Here, all the method steps have been considered in determining that the resulting product must necessarily be a chimeric chicken. If all words in the claim must be considered, then the method steps cannot be ignored. Thus, in keeping with Applicants' cited case law (*Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir 1987)), every element in the claim has been considered in determining that the claimed product must be a chimeric or a transgenic chimeric chicken.

Therefore, the rejection is maintained for reasons of record and the foregoing commentary.

Response & Maintained Claim Rejections - 35 USC § 103

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sang et al. (U.S. Patent Application Publication 2005/0273872), as evidenced by Kamachi et al. (Development 125:2521-2532; 1998), in view of Rapp, J. (U.S. Patent Publication No. 2002/0108132, effective filing date Feb. 2, 2001). It should be noted that the rejection set forth in the previous office action dated October 3, 2008 contained a typographical error on page 5, indicating the rejection of claim 5-15 and 18. However, as is clear in the body of the rejection, and especially on page 6, limitations of claims 2-4 are expressly addressed and indicated as pertinent to each of claims 2-4. Further, claims 7-15 and 18 are withdrawn claims and were not examined. This is further evidenced by the conclusory statement on page 8, indicating the rejection of only claims 1-6 and 25-27, and yet further supported in the Office Action Summary page. The rejection of claim 1-6 is maintained for reasons of record.

Applicants disagree and traverse the rejection, arguing Sang et al. disclose inoculation of chicken embryos at any of stages X-XIII, i.e., blastodermic stages. In contrast, the transgenic bird of the instantly claimed invention is produced by microinjection of a MMLV-derived vector "at a stage except for and after the blastodermic stage just after egg laying," i.e., just after egg laying and after the blastodermic stage.

Applicants' arguments have been fully considered, but are not deemed persuasive. As specifically indicated in the previous office action, Stage 13 chick embryos include the gastrula stage, i.e. up to and including 48 hours; such is evidenced by Kamachi et al. in describing the expression of the lens-specific crystallin gene in the developing chicken (first column, under summary; limitation of claims 2 and 3). Applicants appear to have selectively ignored the foregoing.

Applicants argue that this specific post-blastodermic inoculation imparts distinct and nonobvious structural characteristics to the resulting G1 transgenic bird or transgenic progeny thereof, or egg thereof. Specifically, by performing microinjection of the claimed MMLV-

derived vector after the blastodermic stage, just after egg laying, transgene expression is not subject to gene silencing, thus preventing down-regulation of expression of the transgene. As a consequence of microinjection at this specific developmental stage, the transgenic bird, and egg thereof, of the present invention exhibits unexpectedly superior transgene expression, i.e., the claimed process steps impart an entirely unexpected and non-obvious structural difference vis-a-vis the transgenic birds of Rapp et al. and Sang et al; and refer to Tables 2-4 of the specification, as demonstrating higher protein production than that reported by Rapp et al. and Sang et al.

Such is not found persuasive, because the instant claims do not require the production of proteins of a specified concentration. The claims are directed to a transgenic chicken whose genome comprises a replication-deficient Moloney murine leukemia virus retroviral vector encoding an antibody. Moreover, any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Further, the fact that Applicants have recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Enhanced transgene expression would naturally flow from the process of making a transgenic chicken according to the stage XIII embryos, that include the gastrula stage, because such is a biological phenomenon, inseparable from the organism.

Applicants argue that one of ordinary skill in the art would be strongly discouraged from incorporating the retroviral vector of Rapp et al. into the method of Sang et al., because Sang et al. state that the use of a delivery vector derived from Moloney murine leukemia virus during development leads to gene silencing, and "very low expression of the transgene," and that "it is therefore essential that any viral vector used for production of transgenic birds does not exhibit gene silencing." See paragraph [0016]. Concluding that Sang et al. expressly teaches away from the combination asserted in the rejection, citing *Monarch Knitting Mach. Corp v. Sulzer Morat Gmbh*, 139 F.3d, 877, 45 USPQ2d 1977 (Fed. Cir. 1998); *Para-Ordnance Mfg. v. SGS Importers*

Int'l Inc., 73 F.3d1085, 37 USPQ2d 1237 (Fed. Cir. 1995); and *In re Gurley*, 27 F.3d 551,553 (Fed. Cir. 1994).

Such is not found persuasive, because as previously indicated, the foregoing has been quoted out of context. While Sang et al. state that it is essential that any viral vector used for production of transgenic birds does not exhibit gene silencing, the reference to Moloney murine leukemia virus is from the teachings of Jahner et al. published in 1982, directed to de novo methylation and expression of retroviral genomes during mouse embryogenesis (paragraphs [0016 and 0129]. Therefore, the teachings of Jahner et al. are not necessarily extendable to chickens, especially given the body of subsequent publications with regard to using Moloney murine leukemia virus as an expression vector in chimeric or transgenic birds.

Applicants argue that obvious inquiry is determined based on the knowledge of those of ordinary skill in the art at the time the invention was made. Thus, reliance on subsequent publications, available after the time of the present invention, is clearly improper. Further arguing that at the time of the invention, the art recognized that regulation of gene expression, including gene silencing, during early embryogenesis is highly conserved amongst vertebrates, and as such, one of ordinary skill in the art, at the time of the invention, would have considered that MMLV-derived vectors would also result in transgene silencing in avians.

In response, it is noted that the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. MPEP 716.01(c). Applicants have not provided any evidence to support that MMLV silencing also results in transgene silencing in avians.

Thus, the rejection of claims 1-6 is maintained for reasons of record and the discussion set forth above.

Response & Withdrawn Rejections - Obviousness Type Double Patenting

Claims 1-6 and 25-27 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 41, 44-47 and 49-56 of copending U.S. Patent Application No.: 10/523,191 (2006/0143725; commonly assigned).

Application 10/523,191 has been abandoned, thus rendering the rejection moot. Accordingly, the rejection is hereby withdrawn.

Conclusion

Claims 1-6 and 25-27 are not allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Primary Examiner, Art Unit 1633